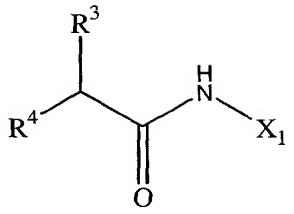
WE CLAIM:

1. A compound of Formula I:



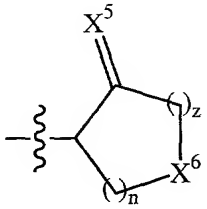
I

in which:

X^1 is $-C(R^1)(R^2)X^2$ or $-X^3$;

X^2 is cyano, -CHO, $-C(R^7)(R^8)R^5$, $-C(R^7)(R^8)CF_3$, $-C(R^7)(R^8)CF_2CF_2R^9$ $-CH{=}CHS(O)_2R^5$, $-C(R^7)(R^8)CF_2C(O)NR^5R^6$, $-C(R^7)(R^8)C(R^7)(R^8)NR^5R^6$, $-C(R^7)(R^8)C(R^7)(R^8)OR^5$, $-C(R^7)(R^8)CH_2OR^5$, $-C(R^7)(R^8)CH_2N(R^6)SO_2R^5$, $-C(R^7)(R^8)C(R^7)(R^8)N(R^6)(CH_2)_2OR^6$, $-C(R^7)(R^8)C(R^7)(R^8)N(R^6)(CH_2)_2NR^6$ or $-C(R^7)(R^8)C(R^7)(R^8)R^5$; wherein R^5 is $(C_{1\text{-}4})$alkyl, $(C_{6\text{-}10})$aryl$(C_{0\text{-}6})$alkyl, hetero$(C_{4\text{-}10})$aryl$(C_{0\text{-}6})$alkyl, $(C_{4\text{-}10})$cycloalkyl$(C_{0\text{-}6})$alkyl or hetero$(C_{4\text{-}10})$cycloalkyl$(C_{0\text{-}6})$alkyl; R^6 is hydrogen or $(C_{1\text{-}6})$alkyl; R^7 is hydrogen or $(C_{1\text{-}4})$alkyl and R^8 is hydroxy or R^7 and R^8 together form oxo; R^9 is hydrogen, halo, $(C_{1\text{-}4})$alkyl, $(C_{5\text{-}10})$aryl$(C_{0\text{-}6})$alkyl or hetero$(C_{5\text{-}10})$aryl$(C_{0\text{-}6})$alkyl;

X^3 represents a group of Formula (a):



(a)

in which n is 1 or 2, z is 0 or 1, X^5 is selected from NR^{10}, S or O, wherein R^{10} is hydrogen or (C_{1-6})alkyl, and X^6 is O, S or NR^{11}, wherein R^{11} is selected from hydrogen, (C_{1-6})alkyl, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4S(O)_2R^{14}$, $-R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4C(O)NR^{12}R^{15}$ and $-X^4S(O)_2NR^{12}R^{15}$, in which X^4 is a bond or (C_{1-6})alkylene; R^{12} at each occurrence independently is hydrogen or (C_{1-6})alkyl; R^{13} is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl, R^{14} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl and R^{15} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-12})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-6})alkyl;

wherein within X^1 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical R^{20} selected from $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{15}R^{12}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$; and wherein X^1 and R^{20} may be substituted further with 1 to 5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$ wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above;

R^1 and R^2 are both fluoro; or

R^1 is hydrogen or (C_{1-6})alkyl and R^2 is selected from the group consisting of hydrogen, (C_{1-6})alkyl, cyano, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$, $-X^4S(O)_2R^{14}$, $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{15}R^{12}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above; or R^1 and R^2 taken together with the carbon atom to which both R^1 and R^2 are attached form (C_{3-8})cycloalkylene or hetero(C_{3-8})cycloalkylene;

wherein R^2, said cycloalkylene and said heterocycloalkylene may be substituted further with 1 to 3 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13} and R^{14} are as defined above;

R^3 and R^4 are independently $-C(R^{16})(R^{17})X^7$, wherein R^{16} and R^{17} are hydrogen, (C_{1-6})alkyl or fluoro, or R^{16} is hydrogen and R^{17} is hydroxy and X^7 is selected from $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$, $-X^4S(O)_2R^{14}$, $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{15}R^{12}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above;

wherein within one of R^3 or R^4 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical R^{21} selected from $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{12}R^{15}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, wherein X^4, R^{12} and R^{15} are as defined above; and wherein each of R^3, R^4 and R^{21} may be substituted further with 1 to 5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13} and R^{14} are as defined above; provided that only one bicyclic ring structure is present within each of R^3 or R^4; and provided that when X^2 is cyano and X^7 within one of R^3 or R^4 is $-X^4C(O)R^{13}$ or $-X^4C(O)R^{15}$, wherein X^4 is a bond, then X^7 within the other of R^3 or R^4 is limited to

$-X^4SR^{15}$, $-X^4S(O)R^{15}$ and $-X^4S(O)_2R^{15}$, wherein R^{15} is (C_{6-10})aryl(C_{1-6})alkyl substituted with 1 to 5 radicals or hetero(C_{5-10})aryl(C_{0-6})alkyl optionally substituted with 1 to 5 radicals, wherein said radicals are independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13} and R^{14} are as defined above, provided that the radical is not selected from only halo when R^{15} is (C_{6-10})aryl(C_{1-6})alkyl; and provided that when X^2 is cyano then X^7 within R^3 and R^4 is not $-X^4C(O)NR^{12}R^{12}$, $-X^4C(O)NR^{15}R^{12}$ or $-X^4C(O)NR^{18}R^{19}$, wherein X^4 is a bond and R^{18} and R^{19} together with the nitrogen atom to which they are attached form hetero(C_{3-10})cycloalkyl or hetero(C_{5-10})aryl;

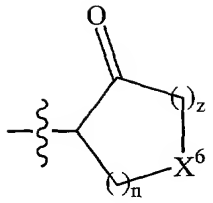
and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

2. The compound of Claim 1 in which:

X^1 is $-C(R^1)(R^2)X^2$ or $-X^3$;

X^2 is cyano, -CHO, $-C(O)R^5$, $-C(O)CF_3$, $-C(O)CF_2CF_2R^9$ $-CH{=}CHS(O)_2R^5$, $-C(O)CF_2C(O)NR^5R^6$, $-C(O)C(O)NR^5R^6$, $-C(O)C(O)OR^5$, $-C(O)CH_2OR^5$, $-C(O)CH_2N(R^6)SO_2R^5$, $-C(O)C(O)N(R^6)(CH_2)_2OR^6$, $-C(O)C(O)N(R^6)(CH_2)_2NR^6$ or $-C(O)C(O)R^5$, wherein R^5 is (C_{1-4})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{4-10})aryl(C_{0-6})alkyl, (C_{4-10})cycloalkyl(C_{0-6})alkyl or hetero(C_{4-10})cycloalkyl(C_{0-6})alkyl, R^6 is hydrogen or (C_{1-6})alkyl and R^9 is halo;

X^3 represents a group of Formula (b):



(b)

in which n is 1 or 2, z is 0 or 1, X^6 is O or NR^{11}, wherein R^{11} is selected from hydrogen, (C_{1-6})alkyl, $-X^4OC(O)R^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4S(O)_2R^{14}$, $-R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4C(O)NR^{12}R^{15}$ and $-X^4S(O)_2NR^{12}R^{15}$, in which X^4 is a bond or (C_{1-6})alkylene; R^{12} at each occurrence independently is hydrogen or (C_{1-6})alkyl; R^{13} is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl, R^{14} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl and R^{15} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-12})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-6})alkyl;

wherein within X^1 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical selected from $-R^{15}$ and $-X^4C(O)R^{15}$; and wherein X^1 may be substituted further with 1 to 3 radicals independently selected from (C_{1-6})alkyl, halo-substituted(C_{1-4})alkyl, $-X^4NR^{12}R^{12}$, $-X^4OR^{13}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above;

R^1 and R^2 are both fluoro; or

R^1 is hydrogen or (C_{1-6})alkyl and R^2 is selected from the group consisting of hydrogen, (C_{1-6})alkyl, $-X^4OR^{13}$ and $-R^{15}$; or R^1 and R^2 taken together with the carbon atom to which both R^1 and R^2 are attached form (C_{3-8})cycloalkylene or hetero(C_{3-8})cycloalkylene; wherein R^2 may be substituted further with (C_{1-6})alkyl; wherein X^4, R^{13} and R^{15} are as defined above;

R^3 and R^4 are independently $-C(R^{16})(R^{17})X^7$, wherein R^{16} and R^{17} are hydrogen, (C_{1-6})alkyl or fluoro, or R^{16} is hydrogen and R^{17} is hydroxy and X^7 is selected from $-X^4SR^{13}$, $-X^4C(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$ and $-X^4C(O)NR^{15}R^{12}$, wherein X^4, R^{12}, R^{13} and R^{15} are as defined above;

wherein within one of R^3 or R^4 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical selected from $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{12}R^{15}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, wherein X^4, R^{12} and R^{15} are as defined above; and wherein each of R^3 and R^4 may be substituted further with 1 to 5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13} and R^{14} are as defined above;

wherein within one of R^3 and R^4 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical selected from $-R^{15}$ and $-X^4OR^{15}$; and wherein each of R^3 or R^4 may be substituted further by 1-5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, $-X^4NR^{12}C(O)OR^{12}$, $-X^4OR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

3. A compound of claim 2 in which R^3 and R^4 are independently $-CH_2X^7$, wherein X^7 is selected from X^4SR^{13}, $-X^4C(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$ and $-X^4C(O)NR^{15}R^{12}$, wherein X^4 is a bond or (C_{1-6})alkylene, R^{12} at each occurrence independently is hydrogen or (C_{1-6})alkyl, R^{13} is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl, R^{14} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl and R^{15} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-12})bicycloaryl(C_{0-6})alkyl or

hetero(C_{8-12})bicycloaryl(C_{0-6})alkyl; wherein within R^3 and R^4 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical selected from $-R^{15}$ and $-X^4OR^{15}$, wherein X^4 and R^{15} are as defined above; and wherein R^3 and R^4 may be substituted further by 1 to 5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, $-X^4NR^{12}C(O)OR^{12}$, $-X^4OR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$ and $-X^4S(O)_2R^{14}$, wherein X^4 R^{12}, R^{13} and R^{14} are as defined above;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

4. A compound of claim 3 in which R^3 is selected from 5-bromo-thiophen-2-ylmethyl, 3-cyclohexylpropyl, 2-cyclohexylpropyl, 2-cyclopentylpropyl, 3-phenylpropyl, 3-(2-difluoromethoxy)phenylpropyl, 2-phenylcyclopropylmethyl, 2,2-difluoro-3-phenylpropyl, 1-benzylcyclopropylmethy, 2-tetrahydro-pyran-4-ylethyl, 1-isobutylcyclopropylmethyl, thiophen-2-ylmethyl, tetrahydro-pyran-4-ylmethyl, cyclopropylmethylsulfanylmethyl, 2,2-dimethyl-3-phenylpropyl, 4-methyl-[1,2,5]thiadiazol-3-ylmethylsulfonylmethyl, 3-methyl-[1,2,4]thiadiazol-3-ylmethylsulfonylmethyl, thiophen-3-ylmethylsulfonylmethyl, 3-methoxy-5-methyl-isoxazol-4-ylmethylsulfonylmethyl, 2,4-dimethyl-thiazol-5-ylmethylsulfonylmethyl, 2-methyl-oxazol-4-ylmethylsulfonylmethyl, 2-methyl-thiazol-4-ylmethylsulfonylmethyl,, 1,2,3]thiadiazol-4-ylmethylsulfonylmethyl, 3-methyl-[1,2,4]thiadiazol-5-ylmethylsulfonylmethyl, 4-methyl-[1,2,5]thiadiazol-3-ylmethylsulfonylmethyl, thiophen-3-ylmethylsulfonylmethyl, tetrahydro-pyran-4-yloxymethyl, piperidin-1-ylcarbonyl, thiophene-2-sulfonylmethyl, 3-chloro-2-fluoro-benzylsulfonylmethyl, benzenesulfonylmethyl, benzylsulfonylmethyl, 2-(1,1-difluoro-methoxy)-benzylsulfonylmethyl, 2-benzenesulfonyl-ethyl, 2-(pyridine-2-sulfonyl)-ethyl, 2-(pyridine-4-sulfonyl)-ethyl, 2-benzylsulfonyl-ethyl, oxy-pyridin-2-ylmethylsulfonylmethyl, prop-2-ene-1-sulfonylmethyl, 4-methoxy-benzylsulfonylmethyl, *p*-tolylmethylsulfonylmethyl,

4-chloro-benzylsulfonylmethyl, *o*-tolylmethylsulfonylmethyl, 3,5-dimethyl-benzylsulfonylmethyl, 4-trifluoromethyl-benzylsulfonylmethyl, 4-trifluoromethoxy-benzylsulfonylmethyl, 2-bromo-benzylsulfonylmethyl, pyridin-2-ylmethylsulfonylmethyl, pyridin-3-ylmethylsulfonylmethyl, pyridin-4-ylmethylsulfonylmethyl, naphthalen-2-ylmethylsulfonylmethyl, 3-methyl-benzylsulfonylmethyl, 3-trifluoromethyl-benzylsulfonylmethyl, 3-trifluoromethoxy-benzylsulfonylmethyl, 4-fluoro-2-trifluoromethoxy-benzylsulfonylmethyl, 2-fluoro-6-trifluoromethyl-benzylsulfonylmethyl, 3-chloro-benzylsulfonylmethyl, 2-fluoro-benzylsulfonylmethyl, 2-trifluoro-benzylsulfonylmethyl, 2-cyano-benzylsulfonylmethyl, 4-*tert*-butyl-benzylsulfonylmethyl, 2-fluoro-3-methyl-benzylsulfonylmethyl, 3-fluoro-benzylsulfonylmethyl, 4-fluoro-benzylsulfonylmethyl, 2-chloro-benzylsulfonylmethyl, 2,5-difluoro-benzylsulfonylmethyl, 2,6-difluoro-benzylsulfonylmethyl, 2,5-dichloro-benzylsulfonylmethyl, 3,4-dichloro-benzylsulfonylmethyl, 2-(1,1-difluoro-methoxy)-benzylsulfonylmethyl, 2-cyano-benzylsulfonylmethyl, 3-cyano-benzylsulfonylmethyl, 2-trifluoromethoxy-benzylsulfonylmethyl, 2,3-difluoro-benzylsulfonylmethyl, 2,5-difluoro-benzylsulfonylmethyl, biphenyl-2-ylmethylsulfonylmethyl, cyclohexylmethyl, 3-fluoro-benzylsulfonylmethyl, 3,4-difluoro-benzylsulfonylmethyl, 2,4-difluoro-benzylsulfonylmethyl, 2,4,6-trifluoro-benzylsulfonylmethyl, 2,4,5-trifluoro-benzylsulfonylmethyl, 2,3,4-trifluoro-benzylsulfonylmethyl, 2,3,5-trifluoro-benzylsulfonylmethyl, 2,5,6-trifluoro-benzylsulfonylmethyl, 2-chloro-5-trifluoromethylbenzylsulfonylmethyl, 2-methyl-propane-1-sulfonyl, 2-fluoro-3-trifluoromethylbenzylsulfonylmethyl, 2-fluoro-4-trifluoromethylbenzylsulfonylmethyl, 2-fluoro-5-trifluoromethylbenzylsulfonylmethyl, 4-fluoro-3-trifluoromethylbenzylsulfonylmethyl, 2-methoxy-benzylsulfonylmethyl, 3,5 bis-trifluoromethyl-benzylsulfonylmethyl, 4-difluoromethoxy-benzylsulfonylmethyl, 2-difluoromethoxy-benzylsulfonylmethyl, 3-difluoromethoxy-benzylsulfonylmethyl, 2,6-dichloro-benzylsulfonylmethyl, biphenyl-4-ylmethylsulfonylmethyl, 3,5-dimethyl-isoxazol-4-ylmethylsulfonylmethyl,

5-chloro-thiophen-2-ylmethylsulfonylmethyl,
2-[4-(1,1-Difluoro-methoxy)-benzenesulfonyl]-ethyl,
2-[2-(1,1-Difluoro-methoxy)-benzenesulfonyl]-ethyl,
2-[3-(1,1-Difluoro-methoxy)-benzenesulfonyl]-ethyl,
2-(4-trifluoromethoxy-benzenesulfonyl)-ethyl,
2-(3-trifluoromethoxy-benzenesulfonyl)-ethyl,
2-(2-trifluoromethoxy-benzenesulfonyl)-ethyl, (cyanomethyl-methyl-carbamoyl)-methyl, biphenyl-3-ylmethyl, 2-oxo-2-pyrrolidin-1-yl-ethyl, 2-benzenesulfonyl-ethyl, isobutylsulfanylmethyl, 2-phenylsulfanyl-ethyl, cyclohexylmethylsulfonylmethyl, 2-cyclohexyl-ethanesulfonyl, benzyl, naphthalen-2-yl, benzylsulfanylmethyl, 2-trifluoromethyl-benzylsulfanylmethyl, phenylsulfanyl-ethyl and cyclopropylmethylsulfonylmethyl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

5. A compound of claim 4 in which R^4 is selected from 2-trifluorobenzylsulfonylmethyl, 3-phenylsulfanylpropyl, 4-chlorobenzylsulfonylmethyl, thiophen-2-ylsulfonylmethyl, benzylsulfonylmethyl, 4-methylbenzylsulfonylmethyl, 2-phenylsulfonylethyl, 2-pyridin-2-ylsulfonylethyl, 2-pyridin-4-ylsulfonylethyl, 2-benzylsulfonylethyl, 2-(3-difluoromethoxyphenylsulfonyl)ethyl, naphthalen-2-ylmethylsulfonylmethyl, pyridin-2-ylmethylsulfonylmethyl, 3-methylbenzylsulfonylmethyl, 3-trifluoromethylbenzylsulfonylmethyl, 3-difluoromethoxybenzylsulfonylmethyl, 3-chlorobenzylsulfonylmethyl, 3-fluorobenzylsulfonylmethyl, 4-fluorobenzylsulfonylmethyl, 3-cyanobenzylsulfonylmethyl, 4-cyanobenzylsulfonylmethyl, 3,4-difluorobenzylsulfonylmethyl, benzylsulfonylmethyl, *N*-cyanomethyl-*N*-methylcarbamoylmethyl, 3-bromobenzyl, 4-phenylbutyl, 2,2-difluoro-3-phenylpropyl, 4'-methylsulfonylaminobiphenyl-3-ylmethyl, 4'-ethoxycarbonylaminobiphenyl-3-ylmethyl, 4-methylpiperazin-1-ylcarbonylmethyl,

1-fluoro-2-(4-methylpiperazin-1-yl)-2-oxoethyl, 1-hydroxy-4-methylpiperazin-1-yl-2-oxoethyl, 1-hydroxy-2-morpholin-4-yl-2-oxoethyl, 1-hydroxy-2-oxo-2-pyrrolidin-1-yl-ethyl, 1-fluoro-2-oxo-2-pyrrolidin-1-yl-ethyl, 1-fluoro-2-isopropylamino-2-oxoethyl, 1-hydroxy-2-isopropylamino-2-oxoethyl, 1-fluoro-2-oxo-2-piperazin-1-ylethyl, thiophen-3-ylmethylsulfonylmethyl, 4-methyl-[1,2,5]thiadiazol-3-ylmethylsulfonylmethyl, 3-methoxy-5-methyl-isoxazol-4-ylmethylsulfonylmethyl, 2,4-dimethyl-thiazol-5-ylmethylsulfonylmethyl, 2-methyl-oxazol-4-ylmethylsulfonylmethyl, 2-methyl-thiazol-4-ylmethylsulfonylmethyl, 2-([1,2,3]thiadiazol-4-ylmethylsulfonyl)-ethyl, 2-(3-methyl-[1,2,4]thiadiazol-5-ylmethylsulfonyl)-ethyl, 2-oxo-2-phenyl-ethyl, 2-morpholin-4-yl-2-oxo-ethyl, 2-benzenesulfonyl-ethyl, 2-naphthalen-2-yl-2-oxo-ethyl, 2-benzo[1,3]dioxol-5-yl-2-oxo-ethyl, 2-benzo[*b*]thiophen-2-yl-2-oxo-ethyl, 2-biphenyl-4-yl-2-oxo-ethyl, 4-benzylsulfonylmethyl, 2-(3-trifluoromethoxy-benzenesulfonyl)-ethyl, 2-oxo-2-(4-phenoxy-phenyl)-ethyl, 2-(4-hydroxy-phenyl)-2-oxo-ethyl, benzylcarbamoyl-methyl, 4-acetyl-piperazine-1-carboxylic acid ethyl ester, cyclohexylcarbamoylmethyl, 2-(3-Chloro-benzo[*b*]thiophen-2-yl)-2-oxo-ethyl, benzenesulfonylmethyl, 2-oxo-2-thiophen-2-yl-ethyl, 2-oxo-2-thiophen-3-yl-ethyl, naphthalene-2-sulfonylmethyl, 2-(5-methyl-thiophen-2-yl)-2-oxo-ethyl, 2-(3-chloro-thiophen-2-yl)-2-oxo-ethyl, 5-methyl-thiophene-2-sulfonylmethyl, phenylcarbamoylmethyl, (5,6,7,8-tetrahydro-naphthalen-1-ylcarbamoyl)-methyl, (4-carbamoyl-phenylcarbamoyl)-methyl, (3-carbamoyl-phenylcarbamoyl)-methyl, (butyl-methyl-carbamoyl)-methyl, biphenyl-4-ylmethyl, 2-oxo-2-*p*-tolyl-ethyl, 2-(3-fluoro-4-methoxy-phenyl)-2-oxo-ethyl, 2-(4-chloro-phenyl)-2-oxo-ethyl, 2-(4-methoxy-phenyl)-2-oxo-ethyl, 2-oxo-2-(4-trifluoromethoxy-phenyl)-ethyl, 2-(3,4-difluoro-phenyl)-2-oxo-ethyl, 2-(3,4-dimethoxy-phenyl)-2-oxo-ethyl, 2-(4-fluoro-phenyl)-2-oxo-ethyl, 5-methyl-2-oxo-hexyl, 3,5-dimethyl-benzylsulfonylmethyl, 4-trifluoromethyl-benzylsulfonylmethyl; 4-trifluoromethoxy-benzylsulfonylmethyl, isopropylcarbamoyl-methyl, 4-dimethylcarbamoylmethyl, pyridin-4-ylcarbamoylmethyl, pyridin-4-ylmethylsulfonylmethyl, pyridin-3-ylmethylsulfonylmethyl, 3,4-dichloro-benzylsulfonylmethyl, pyridin-3-ylcarbamoylmethyl,

4-methoxy-benzylsulfonylmethyl, 4-chloro-benzylsulfonylmethyl, thiophene-2-sulfonylmethyl, benzylsulfonylmethyl, *p*-tolylmethylsulfonylmethyl, 2-benzenesulfonyl-ethyl, 2-(pyridine-2-sulfonyl)-ethyl, 2-(pyridine-4-sulfonyl)-ethyl, 2-benzylsulfonyl-ethyl, 2-[3-(1,1-Difluoro-methoxy)-benzenesulfonyl]-ethyl, naphthalen-2-ylmethylsulfonylmethyl, pyridin-2-ylmethylsulfonylmethyl, *m*-tolylmethylsulfonylmethyl, 3-trifluoromethyl-benzylsulfonylmethyl, 3-trifluoromethoxy-benzylsulfonylmethyl, 3-chloro-benzylsulfonylmethyl, 3-fluoro-benzylsulfonylmethyl, 4-fluoro-benzylsulfonylmethyl, 3-cyano-benzylsulfonylmethyl, 4-cyano-benzylsulfonylmethyl, 3,4-difluoro-benzylsulfonylmethyl, (cyanomethyl-methyl-carbamoyl)-methyl, 3-bromo-benzyl, 2-oxo-2-pyrrolidin-1-yl-ethyl, 2-(4'-chloro-biphenyl-4-yl)-2-oxo-ethyl, biphenyl-3-ylmethyl, 2-(1,1-difluoro-methoxy)-benzylsulfonylmethyl, 2-(4-methylsulfonylamino-phenyl)-2-oxo-ethyl, 2-oxo-2-piperidin-1-yl-ethyl, 2-(4-methylsulfonyl-piperazin-1-yl)-2-oxo-ethyl, 2-trifluoromethyl-benzylsulfonylmethyl, 4-fluoro-3-trifluoromethyl-benzylsulfonylmethyl, 4-carboxy-benzylsulfonylmethyl, 3,5-bis-trifluoromethyl-benzylsulfonylmethyl, 4-(1,1-difluoro-methoxy)-benzylsulfonylmethyl, 3-(1,1-difluoro-methoxy)-benzylsulfonylmethyl, 5-chloro-thiophen-2-ylmethylsulfonylmethyl, 2-[4-(1,1-difluoro-methoxy)-benzenesulfonyl]-ethyl, 2-(4-trifluoromethoxy-benzenesulfonyl)-ethyl, 2-phenylsulfanyl-ethyl, benzylsulfanylmethyl, 2-trifluoromethyl-benzylsulfanylmethyl, 2-trifluoromethoxy-benzylsulfanylmethyl, 2-cyclohexyl-ethyl and isobutylsulfanylmethyl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

6. The compound of claim 5 in which R^1 is hydrogen or (C_{1-6})alkyl and R^2 is hydrogen, $-X^4OR^{13}$, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{5-10})aryl(C_{0-6})alkyl or (C_{1-6})alkyl; or R^1 and R^2 taken together with the carbon atom to which both R^1 and R^2 are attached form

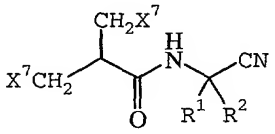
(C_{3-8})cycloalkylene or hetero(C_{3-8})cycloalkylene; wherein the cycloalkylene or heterocycloalkylene are optionally substituted with 1 to 3 (C_{1-6})alkyl radicals;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

7. The compound of claim 6 in which R^1 is hydrogen or methyl and R^2 is methoxymethyl, methoxyethyl, methyl, ethyl, propyl, butyl, phenethyl, hiophen-2-yl or 5-methyl-furan-2-yl; or R^1 and R^2 taken together with the carbon atom to which both R^1 and R^2 are attached form cyclopropyl, tetrahydro-pyran-4-yl or 1-methyl-piperidin-4-yl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

8. The compound of claim 7 of Formula I(a):



I(a)

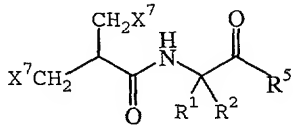
and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

9. The compound of claim 8 selected from the group consisting of 3-biphenyl-3-yl-*N*-cyanomethyl-2-benzylsulfonylmethyl-propionamide; 3-biphenyl-4-yl-*N*-

cyanomethyl-2-benzylsulfonylmethyl-propionamide; 3-(3-bromo-phenyl)-*N*-cyanomethyl-2-benzylsulfonylmethyl-propionamide; *N*-cyanomethyl-3-(3-cyano-benzylsulfonyl)-2-benzylsulfonyl-methyl-propionamide; *N*-cyanomethyl-2-[2-1,1-difluoro-methoxy)-benzylsulfanylmethyl]-3-benzylsulfanyl-propionamide; *N*-cyanomethyl-3-(2-trifluoromethyl-benzylsulfanyl)-2-(2-trifluoro-methyl-benzylsulfanylmethyl)-propionamide; *N*-cyanomethyl-3-isobutylsulfanyl-2-isobutylsulfanylmethyl-propionamide; *N*-cyanomethyl-4-phenylsulfanyl-2-(2-phenylsulfanyl-ethyl)-butyramide; *N*-cyanomethyl-3-[2-(1,1-difluoro-methoxy)-benzylsulfanyl]-2-[2-(1,1-difluoro-methoxy)-benzylsulfanylmethyl]-propionamide; 3-benzylsulfanyl-2-benzylsulfanylmethyl-*N*-cyanomethyl-propionamide; *N*-cyanomethyl-2-[2-1,1-difluoro-methoxy)-benzylsulfonylmethyl]-3-benzylsulfonyl-propionamide; *N*-cyanomethyl-3-(2-trifluoromethyl-benzylsulfonyl)-2-(2-trifluoromethyl-benzylsulfonylmethyl)-propionamide; 4-benzenesulfonyl-2-(2-benzenesulfonyl-ethyl)-*N*-cyanomethyl-butyramide; *N*-cyanomethyl-3-[2-(1,1-difluoro-methoxy)-benzylsulfonyl]-2-[2-(1,1-difluoro-methoxy)-benzylsulfonylmethyl]-propionamide; *N*-cyanomethyl-3-benzylsulfonyl-2-benzylsulfonylmethyl-propionamide; *N*-cyanomethyl-3-(2-methyl-propane-1-sulfonyl)-2-(2-methyl-propane-1-sulfonylmethyl)-propionamide; *N*-cyanomethyl-3-(2-methyl-thiazol-4-ylmethylsulfonyl)-2-benzyl-sulfonylmethyl-propionamide; 3-biphenyl-3-yl-*N*-cyanomethyl-2-[2-(1,1-difluoro-methoxy)-benzyl-sulfonylmethyl]-propionamide; (3'-{2-(cyanomethyl-carbamoyl)-3-[2-(1,1-difluoro-methoxy)-benzyl-sulfonyl]-propyl}-biphenyl-4-yl)-carbamic acid ethyl ester; *N*-cyanomethyl-2-[2-(1,1-difluoro-methoxy)-benzylsulfonylmethyl]-3-(4'-methylsulfonylamino-biphenyl-3-yl)-propionamide; 3-(3-bromo-phenyl)-*N*-cyanomethyl-2-[2-(1,1-difluoro-methoxy)-phenyl-methylsulfonylmethyl]-propionamide; *N*-cyanomethyl-2-((E)-3-phenyl-allyl)-3-benzylsulfonyl-propionamide; and *N*-cyanomethyl-3-benzylsulfonyl-2-(3-phenyl-propyl)-propionamide;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

10. The compound of Claim 7 of Formula I(b):



I(b)

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

11. The compound of claim 10 in which R^5 is 1*H*-benzoimidazol-2-yl, benzooxazol-2-yl, oxazolo[4,5-b]pyridin-2-yl, benzothiazol-2-yl, 5-phenyl-[1,3,4]oxadiazol-2-yl, 4-(5-pyridin-4-yl-[1,3,4]oxadiazol-2-yl, 5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl, 5-pyridazin-3-yl-[1,3,4]oxadiazol-2-yl, pyrimidin-2-yl, pyridazin-3-yl, 3-penyl-[1,2,4]oxadiazol-5-yl, 5-methoxymethyl-[1,3,4]oxadiazol-2-yl, 5-ethyl-[1,3,4]oxadiazol-2-yl,, 1,3,4]thiadiazol-2-yl, benzyloxycarbonyl, benzyloxydicarbonyl, phenyldicarbonyl, 5-methyl-[1,3,4]thiadiazol-2-yl, 5-trifluoromethyl-[1,3,4]oxadiazol-2-yl, 5-methyl-[1,3,4]oxadiazol-2-yl, 5-methyl-[1,2,4]oxadiazol-3-yl, 5-phenyl-[1,2,4]oxadiazol-3-yl, 5-thiophen-3-yl-[1,2,4]oxadiazol-3-yl, 5-trifluoromethyl-[1,2,4]oxadiazol-3-yl, 3-methyl-[1,2,4]oxadiazol-5-yl or 3-pyrazin-2-yl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

12. The compound of claim 11 selected from the group consisting of *N*-[(S)-1-(1-Benzooxazol-2-yl-methanoyl)-butyl]-3-benzylsulfonyl-2-benzylsulfonylmethyl-propionamide; *N*-[(S)-1-(1-Benzooxazol-2-yl-methanoyl)-butyl]-3-(2-trifluoromethyl-benzylsulfonyl)-2-(2-trifluoromethyl-benzylsulfonylmethyl)-propionamide; *N*-[(S)-1-(1-

Benzooxazol-2-yl-methanoyl)-pentyl]-4-(2-methoxy-benzenesulfonyl)-2-[2-(2-methoxy-benzenesulfonyl)-ethyl]-butyramide; 4-Benzenesulfonyl-2-(2-benzenesulfonyl-ethyl)-*N*-[(S)-1-(1-benzooxazol-2-yl-methanoyl)-butyl]-butyramide; (R)-*N*-[(S)-1-(1-benzooxazol-2-yl-methanoyl)-butyl]-2-cyclohexylmethyl-3-benzylsulfonyl-propionamide; *N*-[(S)-1-(1-benzothiazol-2-yl-methanoyl)-propyl]-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-[(S)-1-(1-benzooxazol-2-yl-methanoyl)-butyl]-3-cyclohexyl-2-cyclohexylmethyl-propionamide; *N*-[(S)-1-(1-Benzooxazol-2-yl-methanoyl)-butyl]-3-isobutylsulfanyl-2-isobutylsulfanylmethyl-propionamide; *N*-[(S)-1-(1-benzooxazol-2-yl-methanoyl)-butyl]-3-benzylsulfanyl-2-benzylsulfanylmethyl-propionamide; *N*-[(S)-1-(1-benzooxazol-2-yl-methanoyl)-butyl]-4-phenylsulfanyl-2-(2-phenylsulfanyl-ethyl)-butyramide; *N*-[(S)-1-(1-benzooxazol-2-yl-methanoyl)-propyl]-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-[(S)-1-(1-Benzooxazol-2-yl-methanoyl)-pentyl]-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; 4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-*N*-{(S)-1-[1-(3-phenyl-[1,2,4]oxadiazol-5-yl)-methanoyl]-propyl}-butyramide; *N*-[(S)-1-(1-Benzooxazol-2-yl-methanoyl)-butyl]-2-[2-(1,1-difluoro-methoxy)-benzylsulfonylmethyl]-3-benzylsulfonyl-propionamide; 4-Morpholin-4-yl-4-oxo-*N*-[1-(2-oxo-2-phenyl-acetyl)-pentyl]-2-benzylsulfonylmethyl-butyramide; *N*-(1,1-Dimethyl-2-oxazolo[4,5-b]pyridin-2-yl-2-oxo-ethyl)-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-[1-(5-Ethyl-[1,3,4]oxadiazole-2-carbonyl)-butyl]-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-[1-(5-Ethyl-[1,3,4]oxadiazole-2-carbonyl)-butyl]-4-oxo-2-benzylsulfonyl-methyl-4-piperidin-1-yl-butyramide; *N*-[1-(5-Ethyl-[1,3,4]oxadiazole-2-carbonyl)-butyl]-4-oxo-2-benzylsulfonyl-methyl-4-pyrrolidin-1-yl-butyramide; *N*-[1-(5-Methoxymethyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-[1-(5-Methoxymethyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-4-oxo-2-benzylsulfonylmethyl-4-piperidin-1-yl-butyramide; *N*-[1-(5-Methoxymethyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-4-oxo-2-benzylsulfonylmethyl-4-pyrrolidin-1-yl-butyramide; 4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-*N*-[1-(5-phenyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-butyramide; 4-Oxo-2-benzylsulfonylmethyl-*N*-[1-(5-phenyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-4-piperidin-1-yl-butyramide; 4-Oxo-2-benzylsulfonylmethyl-*N*-[1-(5-phenyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-4-pyrrolidin-1-yl-butyramide; 4-Morpholin-4-yl-*N*-

[1-(oxazolo[4,5-b]pyridine-2-carbonyl)-propyl]-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-[1-(Oxazolo[4,5-b]pyridine-2-carbonyl)-propyl]-4-oxo-2-benzylsulfonyl-methyl-4-piperidin-1-yl-butyramide; *N*-[1-(Oxazolo[4,5-b]pyridine-2-carbonyl)-propyl]-4-oxo-2-benzylsulfonyl-methyl-4-pyrrolidin-1-yl-butyramide; 4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-*N*-[1-(5-pyridin-4-yl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-butyramide; 4-Oxo-2-benzylsulfonylmethyl-4-piperidin-1-yl-*N*-[1-(5-pyridin-4-yl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-butyramide; 4-Oxo-2-benzylsulfonylmethyl-*N*-[1-(5-pyridin-4-yl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-4-pyrrolidin-1-yl-butyramide; 4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-*N*-[1-(5-pyridin-3-yl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-butyramide; *N*-[1-(Benzooxazole-2-carbonyl)-propyl]-4-oxo-2-benzylsulfonylmethyl-4-piperidin-1-yl-butyramide; *N*-[1-(Benzooxazole-2-carbonyl)-propyl]-4-oxo-2-benzylsulfonylmethyl-4-pyrrolidin-1-yl-butyramide; *N*-[1-(Benzooxazole-2-carbonyl)-propyl]-2-cyclohexylmethyl-4-morpholin-4-yl-4-oxo-butyramide; 2-Cyclohexylmethyl-4-morpholin-4-yl-*N*-[1-(oxazolo[4,5-b]pyridine-2-carbonyl)-propyl]-4-oxo-butyramide; 2-Cyclohexylmethyl-N-[1-(5-ethyl-[1,3,4]oxadiazole-2-carbonyl)-butyl]-4-morpholin-4-yl-4-oxo-butyramide; *N*-(2-Benzooxazol-2-yl-1-methoxymethyl-2-oxo-ethyl)-2-(2-difluoromethoxy-benzylsulfonylmethyl)-4-morpholin-4-yl-4-oxo-butyramide; *N*-[1-(Benzooxazole-2-carbonyl)-propyl]-2-(2-cyclohexyl-ethyl)-4-morpholin-4-yl-4-oxo-butyramide; 2-(2-Cyclohexyl-ethyl)-4-morpholin-4-yl-*N*-[1-(oxazolo[4,5-b]pyridine-2-carbonyl)-propyl]-4-oxo-butyramide; 2-(2-Cyclohexyl-ethyl)-4-morpholin-4-yl-4-oxo-*N*-[1-(5-phenyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-butyramide; 2-(2-Difluoromethoxy-benzylsulfonylmethyl)-4-morpholin-4-yl-4-oxo-*N*-[1-(5-phenyl-[1,3,4]oxadiazole-2-carbonyl)-propyl]-butyramide; 2-(2-Difluoromethoxy-benzylsulfonylmethyl)-*N*-[1-(5-ethyl-[1,3,4]oxadiazole-2-carbonyl)-butyl]-4-morpholin-4-yl-4-oxo-butyramide; *N*-[1-(Benzooxazole-2-carbonyl)-propyl]-2-(2-difluoromethoxy-benzyl-sulfonylmethyl)-4-morpholin-4-yl-4-oxo-butyramide;

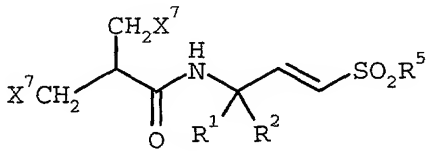
2-(2-Morpholin-4-yl-2-oxo-ethyl)-5-phenyl-pentanoic acid, 1-(benzooxazole-2-carbonyl)-propyl]-amide; (R)-2-Cyclohexylmethyl-4-morpholin-4-yl-4-oxo-*N*-[(S)-1-(5-phenyl-1,2,4-oxadiazole-3-carbonyl)-propyl]-butyramide; 2-(2-Morpholin-4-yl-2-oxo-ethyl)-5-phenyl-pentanoic acid, (S)-1-(5-phenyl-[1,2,4]oxadiazole-3-carbonyl)-propyl]-amide; 4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-*N*-[(S)-1-(5-phenyl-1,2,4-

oxadiazole-3-carbonyl)-propyl]-butyramide; (R)-2-Cyclohexylmethyl-4-morpholin-4-yl-4-oxo-*N*-[(S)-1-(3-phenyl-1,2,4-oxadiazole-5-carbonyl)-propyl]-butyramide; 4-Morpholin-4-yl-*N*-[1-(oxazole-2-carbonyl)-3-phenyl-propyl]-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-(1,1-Dimethyl-2-oxazol-2-yl-2-oxo-ethyl)-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-4-Isopropyl-*N*-1-[1-(oxazole-2-carbonyl)-3-phenyl-propyl]-2-benzylsulfonylmethyl-succinamide; 2-(2-Difluoromethoxy-benzylsulfonylmethyl)-4-morpholin-4-yl-*N*-[1-(oxazole-2-carbonyl)-3-phenyl-propyl]-4-oxo-butyramide; 2-(2-Methyl-propane-1-sulfonylmethyl)-4-morpholin-4-yl-*N*-[1-(oxazole-2-carbonyl)-3-phenyl-propyl]-4-oxo-butyramide; 2-Cyclopropylmethylsulfonylmethyl-4-morpholin-4-yl-*N*-[1-(oxazole-2-carbonyl)-3-phenyl-propyl]-4-oxo-butyramide; *N*-[1-(Benzooxazole-2-carbonyl)-butyl]-2-benzylsulfonyl-3-(tetrahydro-pyran-4-yloxymethyl)-propionamide; *N*-[1-(Benzooxazole-2-carbonyl)-butyl]-3-ethanesulfonyl-2-(tetrahydro-pyran-4-yloxymethyl)-propionamide; *N*-(1-Benzenesulfonyl-3-oxo-azepan-4-yl)-2-cyclopropylmethylsulfonyl-methyl-4-morpholin-4-yl-4-oxo-butyramide; 2-Cyclopropylmethylsulfonylmethyl-N-{(S)-1-[(R)-hydroxy-(3-phenyl-1,2,4-oxadiazol-5-yl)-methyl]-propyl}-4-morpholin-4-yl-4-oxo-butyramide; *N*-{(S)-1-[(R)-hydroxy-(3-phenyl-1,2,4-oxadiazol-5-yl)-methyl]-propyl}-2-(2-methyl-propane-1-sulfonylmethyl)-4-morpholin-4-yl-4-oxo-butyramide; 2-(2-Morpholin-4-yl-2-oxo-ethyl)-5-phenyl-pentanoic acid {(S)-1-[(R)-hydroxy-(3-phenyl-1,2,4-oxadiazol-5-yl)-methyl]-propyl}-amide; 2-Cyclopropylmethylsulfonylmethyl-4-morpholin-4-yl-4-oxo-N-[(S)-1-(3-phenyl-1,2,4-oxadiazole-5-carbonyl)-propyl]-butyramide; 2-(2-methyl-propane-1-sulfonylmethyl)-4-morpholin-4-yl-4-oxo-N-[(S)-1-(3-phenyl-1,2,4-oxadiazole-5-carbonyl)-propyl]-butyramide; 2-(2-Morpholin-4-yl-2-oxo-ethyl)-5-phenyl-pentanoic acid, (S)-1-(3-phenyl-1,2,4-oxadiazole-5-carbonyl)-propyl}-amide; *N*-[(1S)-1-(Benzooxazol-2-yl-hydroxy-methyl)-3-phenyl-propyl]-2-cyclopropylmethylsulfonylmethyl-4-morpholin-4-yl-4-oxo-butyramide; (R)-2-((S)-1-Hydroxy-2-morpholin-4-yl-2-oxo-ethyl)-5-phenyl-pentanoic acid, 1-(benzoxazole-2-carbonyl)-propyl]-amide; (R)-5-(2-Difluoromethoxy-phenyl)-2-((S)-1-hydroxy-2-morpholin-4-yl-2-oxo-ethyl)-pentanoic acid, 1-(benzoxazole-2-carbonyl)-propyl]-amide; and 4-Morpholin-4-yl-N-[1-(oxazole-2-carbonyl)-cyclopropyl]-4-oxo-2-benzylsulfonyl methyl –butyramide;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual

isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

13. The compound of claim 7 of Formula I(c):



I(c)

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

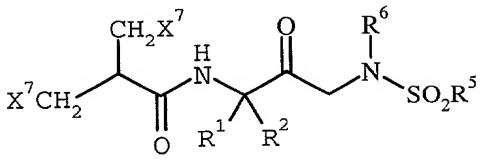
14. The compound of claim 13 in which R^5 is phenyl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

15. The compound of claim 14 selected from the group consisting of *N*-[(S)-1-((E)-2-benzenesulfonyl-vinyl)-pentyl]-3-benzylsulfonyl-2-benzylsulfonylmethyl-propionamide and *N*-(3-benzenesulfonyl-1-phenethyl-allyl)-3-benzylsulfonyl-2-benzylsulfonylmethyl-propionamide;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

16. The compound of claim 7 of Formula I(d):



I(d)

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

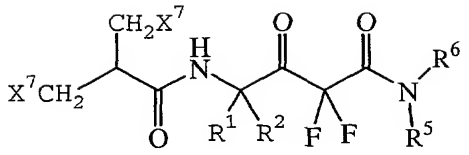
17. The compound of claim 16 in which R^5 is phenyl and R^6 is hydrogen;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

18. The compound of claim 17 namely *N*-(3-benzenesulfonylamino-2-oxo-propyl)-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

19. The compound of claim 7 of Formula I(e):



I(e)

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

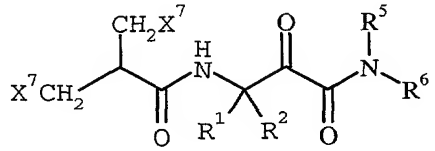
20. The compound of claim 19 in which R^5 and R^6 is methyl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

21. The compound of claim 20 in which one X^7 is morpholine-4-carbonyl and the other is benzylsulfonyl, R^1 is hydrogen and R^2 is ethyl, namely (S)-2,2-difluoro-4-(4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butanoylamino)-3-oxo-hexanoic acid dimethylamide;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

22. The compound of claim 7 of Formula I(f):



and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

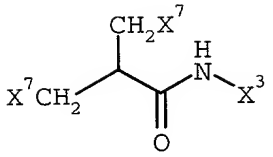
23. The compound of claim 22 in which R^5 is methyl, benzyl, phenethyl, cyclohexyl, methoxyethyl, dimethylaminoethyl, tetrahydro-pyran-4-yl, 1-methylsulfonyl-piperidin-4-yl, 4-methyl-piperazin-1-yl, morpholin-4-ylethyl, pyridin-2-yl, pyridin-2-ylmethyl or oxazol-2-ylmethyl; R^6 is hydrogen or methyl; or R^5 and R^6 together with the nitrogen atom to which both R^5 and R^6 are attached form morpholine-4-yl, pyrrolidin-1-yl, 4-dimethylamino-piperazin-1-yl, 4-hydroxy-piperazin-1-yl, 4-pyridin-2-yl-piperazin-1-yl, 4-benzoyl-piperazin-1-yl or 3-oxo-piperazin-1-yl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

24. The compound of claim 23 selected from the group consisting of *N*-[(S)-1-(1-Benzylcarbamoyl-methanoyl)-propyl]-3-benzylsulfonyl-2-benzylsulfonylmethyl-propionamide and *N*-[(S)-1-(1-Benzylcarbamoyl-methanoyl)-propyl]-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

25. The compound of claim 7 of Formula I(g):



I(g)

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

26. The compound of claim 25 in which X^3 is 1-benzoyl-4-oxo-pyrrolidin-3-yl, 4-oxo-pyrrolidin-3-yl-1-carboxylic acid tert-butyl ester, 2-methyl-4-oxo-tetrahydro-furan-3-yl, 2-ethyl-4-oxo-tetrahydro-furan-3-yl, 4-oxo-tetrahydro-furan-3-yl, 2-acetoxy-4-oxo-azetidin-3-yl, 1-isopropyl-3-oxo-azepan-4-yl, 3-oxo-azepan-4-yl-1-carboxylic acid benzyl ester, 3-oxo-azepan-4-yl-1-carboxylic acid tert-butyl ester, 1-benzoyl-3-oxo-azepan-4-yl, 1-isobutyryl-3-oxo-azepan-4-yl, 3-oxo-1-(propane-2-sulfonyl)-azepan-4-yl, 1-benzenesulfonyl-3-oxo-azepan-4-yl, 1-benzenesulfonyl-3-oxo-piperidin-4-yl, 1-benzenesulfonyl-4-oxo-pyrrolidin-3-yl, 1-benzoyl-3-oxo-piperidin-4-yl or 3-oxo-tetrahydro-pyran-4-yl;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

27. The compound of claim 23 selected from the group consisting of 3-Hydroxy-4-(4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyrylamino)-azepane-1-carboxylic acid tert-butyl ester; 4-(2-Cyclopropylmethylsulfonylmethyl-4-morpholin-4-yl-4-oxo-butyrylamino)-3-hydroxy-azepane-1-carboxylic acid tert-butyl ester; 3-Hydroxy-4-[2-(2-methyl-propane-1-sulfonylmethyl)-4-morpholin-4-yl-4-oxo-butyrylamino]-azepane-1-carboxylic acid tert-butyl ester; 4-(4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-

butyrylamino)-3-oxo-azepane-1-carboxylic acid tert-butyl ester; 4-(2-Cyclopropylmethylsulfonylmethyl-4-morpholin-4-yl-4-oxo-butyrylamino)-3-oxo-azepane-1-carboxylic acid tert-butyl ester; 4-[2-(2-Methyl-propane-1-sulfonylmethyl)-4-morpholin-4-yl-4-oxo-butyrylamino]-3-oxo-azepane-1-carboxylic acid tert-butyl ester; *N*-(1-Benzenesulfonyl-3-oxo-azepan-4-yl)-4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyramide; *N*-(1-Benzenesulfonyl-3-oxo-azepan-4-yl)-2-(2-methyl-propane-1-sulfonylmethyl)-4-morpholin-4-yl-4-oxo-butyramide; 3-(4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyrylamino)-4-oxo-pyrrolidine-1-carboxylic acid tert-butyl ester; 4-(4-Morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butyrylamino)-3-oxo-azepane-1-carboxylic acid benzyl ester; and acetic acid (2S,3S)-3-(4-morpholin-4-yl-4-oxo-2-benzylsulfonylmethyl-butanoylamino)-4-oxo-azetidin-2-yl ester;

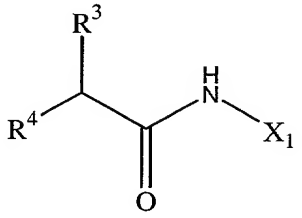
and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds and the N-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

28. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a pharmaceutically acceptable excipient.

29. A method for treating a disease in an animal in which inhibition of Cathepsin S can prevent, inhibit or ameliorate the pathology and/or symptomology of the disease, which method comprises administering to the animal a therapeutically effective amount of compound of Claim 1 or a *N*-oxide derivative or individual isomer or mixture of isomers thereof; or a pharmaceutically acceptable salt or solvate of such compounds and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual isomers and mixtures of isomers thereof.

30. The use of a compound of Claim 1 in the manufacture of a medicament for treating a disease in an animal in which Cathepsin S activity contributes to the pathology and/or symptomology of the disease.

31. A process for preparing a compound of Formula I:



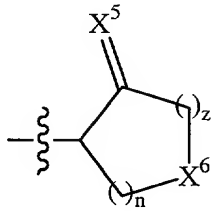
I

in which:

X^1 is $-C(R^1)(R^2)X^2$ or $-X^3$;

X^2 is cyano, -CHO, $-C(R^7)(R^8)R^5$, $-C(R^7)(R^8)CF_3$, $-C(R^7)(R^8)CF_2CF_2R^9$ $-CH{=}CHS(O)_2R^5$, $-C(R^7)(R^8)CF_2C(O)NR^5R^6$, $-C(R^7)(R^8)C(R^7)(R^8)NR^5R^6$, $-C(R^7)(R^8)C(R^7)(R^8)OR^5$, $-C(R^7)(R^8)CH_2OR^5$, $-C(R^7)(R^8)CH_2N(R^6)SO_2R^5$, $-C(R^7)(R^8)C(R^7)(R^8)N(R^6)(CH_2)_2OR^6$, $-C(R^7)(R^8)C(R^7)(R^8)N(R^6)(CH_2)_2NR^6$ or $-C(R^7)(R^8)C(R^7)(R^8)R^5$; wherein R^5 is $(C_{1\text{-}4})$alkyl, $(C_{6\text{-}10})$aryl$(C_{0\text{-}6})$alkyl, hetero$(C_{4\text{-}10})$aryl$(C_{0\text{-}6})$alkyl, $(C_{4\text{-}10})$cycloalkyl$(C_{0\text{-}6})$alkyl or hetero$(C_{4\text{-}10})$cycloalkyl$(C_{0\text{-}6})$alkyl; R^6 is hydrogen or $(C_{1\text{-}6})$alkyl; R^7 is hydrogen or $(C_{1\text{-}4})$alkyl and R^8 is hydroxy or R^7 and R^8 together form oxo; R^9 is hydrogen, halo, $(C_{1\text{-}4})$alkyl, $(C_{5\text{-}10})$aryl$(C_{0\text{-}6})$alkyl or hetero$(C_{5\text{-}10})$aryl$(C_{0\text{-}6})$alkyl;

X^3 represents a group of Formula (a):



(a)

in which n is 1 or 2, z is 0 or 1, X^5 is selected from NR^{10}, S or O, wherein R^{10} is hydrogen or (C_{1-6})alkyl, and X^6 is O, S or NR^{11}, wherein R^{11} is selected from hydrogen, (C_{1-6})alkyl, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4S(O)_2R^{14}$, $-R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4C(O)NR^{12}R^{15}$ and $-X^4S(O)_2NR^{12}R^{15}$, in which X^4 is a bond or (C_{1-6})alkylene; R^{12} at each occurrence independently is hydrogen or (C_{1-6})alkyl; R^{13} is hydrogen, (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl, R^{14} is (C_{1-6})alkyl or halo-substituted(C_{1-6})alkyl and R^{15} is (C_{3-10})cycloalkyl(C_{0-6})alkyl, hetero(C_{3-10})cycloalkyl(C_{0-3})alkyl, (C_{6-10})aryl(C_{0-6})alkyl, hetero(C_{5-10})aryl(C_{0-6})alkyl, (C_{9-12})bicycloaryl(C_{0-6})alkyl or hetero(C_{8-12})bicycloaryl(C_{0-6})alkyl;

wherein within X^1 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical R^{20} selected from $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{15}R^{12}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$; and wherein X^1 and R^{20} may be substituted further with 1 to 5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$ wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above;

R^1 and R^2 are both fluoro; or

R^1 is hydrogen or (C_{1-6})alkyl and R^2 is selected from the group consisting of hydrogen, (C_{1-6})alkyl, cyano, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$, $-X^4S(O)_2R^{14}$, $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{15}R^{12}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above; or R^1 and R^2 taken together with the carbon atom to which both R^1 and R^2 are attached form (C_{3-8})cycloalkylene or hetero(C_{3-8})cycloalkylene;

wherein R^2, said cycloalkylene and said heterocycloalkylene may be substituted further with 1 to 3 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13} and R^{14} are as defined above;

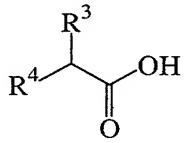
R^3 and R^4 are independently $-C(R^{16})(R^{17})X^7$, wherein R^{16} and R^{17} are hydrogen, (C_{1-6})alkyl or fluoro, or R^{16} is hydrogen and R^{17} is hydroxy and X^7 is selected from $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$, $-X^4S(O)_2R^{14}$, $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{15}R^{12}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, wherein X^4, R^{12}, R^{13}, R^{14} and R^{15} are as defined above;

wherein within one of R^3 or R^4 any cycloalkyl, heterocycloalkyl, aryl or heteroaryl may be substituted with 1 radical R^{21} selected from $-R^{15}$, $-X^4OR^{15}$, $-X^4SR^{15}$, $-X^4S(O)R^{15}$, $-X^4S(O)_2R^{15}$, $-X^4C(O)R^{15}$, $-X^4C(O)OR^{15}$, $-X^4OC(O)R^{15}$, $-X^4NR^{15}R^{12}$, $-X^4NR^{12}C(O)R^{15}$, $-X^4NR^{12}C(O)OR^{15}$, $-X^4C(O)NR^{12}R^{15}$, $-X^4S(O)_2NR^{15}R^{12}$, $-X^4NR^{12}S(O)_2R^{15}$, $-X^4NR^{12}C(O)NR^{15}R^{12}$ and $-X^4NR^{12}C(NR^{12})NR^{15}R^{12}$, wherein X^4, R^{12} and R^{15} are as defined above; and wherein each of R^3, R^4 and R^{21} may be substituted further with 1 to 5 radicals independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13} and R^{14} are as defined above; provided that only one bicyclic ring structure is present within each of R^3 or R^4; and provided that when X^2 is cyano and X^7 within one of R^3 or R^4 is $-X^4C(O)R^{13}$ or $-X^4C(O)R^{15}$, wherein X^4 is a bond, then X^7 within the other of R^3 or R^4 is limited to

$-X^4SR^{15}$, $-X^4S(O)R^{15}$ and $-X^4S(O)_2R^{15}$, wherein R^{15} is (C_{6-10})aryl(C_{1-6})alkyl substituted with 1 to 5 radicals or hetero(C_{5-10})aryl(C_{0-6})alkyl optionally substituted with 1 to 5 radicals, wherein said radicals are independently selected from (C_{1-6})alkyl, cyano, halo, halo-substituted(C_{1-4})alkyl, nitro, $-X^4NR^{12}R^{12}$, $-X^4NR^{12}C(O)R^{12}$, $-X^4NR^{12}C(O)OR^{12}$, $-X^4NR^{12}C(O)NR^{12}R^{12}$, $-X^4NR^{12}C(NR^{12})NR^{12}R^{12}$, $-X^4OR^{13}$, $-X^4SR^{13}$, $-X^4C(O)OR^{12}$, $-X^4C(O)R^{13}$, $-X^4OC(O)R^{13}$, $-X^4C(O)NR^{12}R^{12}$, $-X^4S(O)_2NR^{12}R^{12}$, $-X^4NR^{12}S(O)_2R^{13}$, $-X^4P(O)(OR^{12})OR^{12}$, $-X^4OP(O)(OR^{12})OR^{12}$, $-X^4S(O)R^{14}$ and $-X^4S(O)_2R^{14}$, wherein X^4, R^{12}, R^{13} and R^{14} are as defined above, provided that the radical is not selected from only halo when R^{15} is (C_{6-10})aryl(C_{1-6})alkyl; and provided that when X^2 is cyano then X^7 within R^3 and R^4 is not $-X^4C(O)NR^{12}R^{12}$, $-X^4C(O)NR^{15}R^{12}$ or $-X^4C(O)NR^{18}R^{19}$, wherein X^4 is a bond and R^{18} and R^{19} together with the nitrogen atom to which they are attached form hetero(C_{3-10})cycloalkyl or hetero(C_{5-10})aryl;

and the corresponding N-oxides, and their prodrugs, and their protected derivatives, individual isomers and mixtures of isomers thereof; and the pharmaceutically acceptable salts and solvates of such compounds of formula I and their N-oxides and their prodrugs, and their protected derivatives, individual isomers and mixtures of isomers thereof; which process comprises:

(A) reacting a compound of Formula 2:



2

with a compound of the formula $NH_2CR^1R^2X^2$, in which X^2, R^1, R^2, R^3 and R^4 are as defined in the Summary of the Invention for Formula I; or

(B) reacting a compound of Formula 2 with a compound of the formula NH_2X^3, in which X^3, R^3 and R^4 are as defined in the Summary of the Invention for Formula I; or

(C) optionally converting a compound of Formula I into a pharmaceutically acceptable salt;

(D) optionally converting a salt form of a compound of Formula I to non-salt form;

(E) optionally converting an unoxidized form of a compound of Formula I into a pharmaceutically acceptable *N*-oxide;

(F) optionally converting an *N*-oxide form of a compound of Formula I its unoxidized form;

(G) optionally resolving an individual isomer of a compound of Formula I from a mixture of isomers;

(H) optionally converting a non-derivatized compound of Formula I into a pharmaceutically prodrug derivative; and

(I) optionally converting a prodrug derivative of a compound of Formula I to its non-derivatized form.